



**NTP**  
National Toxicology Program

# Research Strategies and Critical Data Needs: Common Themes

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**Propose a research strategy to explore the **significance** of exposures to environmental chemicals in the rising rates of obesity and diabetes, including human, animal and mechanistic studies**

- This question was not answered

**Are there research avenues that should be avoided?**

- Avoid assumptions that all adult-onset diabetes has a common etiology



## **Are there immediate data gaps that if filled would provide significant direction to longer term research programs?**

- Exposure assessment
  - Expand capacity and improve sensitivity of detection methods
  - Identify chemicals of interest
- Develop/refine high and medium throughput screens
  - Identify chemicals of interest
  - Provide insight into modes of action
  - A tool to assess mixtures
- Identify appropriate animal models



## Research Needs/Strategies

- Use existing cohorts/specimens
  - Consider non-traditional samples (e.g., elective surgeries, fingernail clippings, hair)
- Meta-analysis or pooling from existing and ongoing studies
- Identify better biomarkers
- Collect new samples in a forward thinking manner
- Consider characteristics of animal model system
  - Species differences (e.g., chemical specific pharmacokinetics, PPAR $\alpha$  in rodent and human)
  - Disease state of interest (e.g., Type 1 vs Type 2 diabetes)
  - Genetic diversity of the model



## **Research Needs/Strategies cont.**

- Parallel testing of key compounds and mixtures
- Identify key “causal” pathways for each disease
- Understand role of dietary habits and role in modifying chemical toxicity
- Non-linear responses (low dose vs high dose)
- Identify critical windows of development
- Define role of other factors, e.g., vitamin D status, gut flora



## **Methodology - Measure Most Relevant Endpoints**

- **Animal studies**
  - Obesity: fat mass, fat distribution fat pad, DXA, NMR,
  - Diabetes: blood glucose and insulin (fasting and fed), GTT, ITT,
  - Hormones and metabolic phenotyping (i.e., food intake, energy expenditure)
  - Dietary and genetic background control
- **Human studies**
  - Use diagnostic criteria for fasting glucose, ↑ BMI, ↑ waist/height ratio, hemoglobin A1C, HDL